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July 12, 2007

Date

Sharon V. Hart

**PATENT**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:

Philip E. Thorpe and Sophia Ran (As  
Amended)

Serial No.: 10/621,269

Filed: July 15, 2003

For: Selected Antibody Compositions for  
Binding to Aminophospholipids (As  
Amended)

Group Art Unit: 1642

Examiner: Goddard, L.

Atty. Dkt. No.: 4001.003000

**THIRD DECLARATION OF  
PHILIP E. THORPE UNDER 37 C.F.R. § 1.132**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

I, PHILIP E. THORPE, HEREBY DECLARE AS FOLLOWS:

1. I am a co-inventor of the subject matter disclosed and claimed in the captioned patent application.
2. I am Professor of Pharmacology and hold the Serena S. Simmons Distinguished Chair in Cancer Immunopharmacology at the Simmons Comprehensive Cancer Center, The University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, U.S.A. A copy of my *Curriculum Vitae* is attached as **Exhibit A**.

3. I have reviewed the captioned patent application again. I understand the claims in the captioned patent application to be drawn to purified antibodies, or antigen-binding fragments thereof, which bind to phosphatidylserine (PS), preferably in an ELISA recited in the claims, and have the characteristics as defined in the claims; and to compositions comprising, hybridomas producing and methods for preparing such antibodies.

4. I have reviewed the second Official Action issued by the U.S. Patent and Trademark Office (P.T.O.), the agency charged with assessing the patentability of the captioned patent application. I have also reviewed the documents cited in the second Official Action, including Rote *et al.*, *Clin. Immunol. Immunopathol.*, 66:193-200, 1993 (Rote *et al.*, 1993) and published PCT patent application WO 00/02584, of which I am a co-inventor.

5. I understand that, in the second Official Action, the P.T.O. has taken the position that most claims of the captioned patent application lack novelty over Rote *et al.*, 1993 or WO 00/02584. One particular question that the P.T.O. has raised is whether the antibody termed 3SB9b (now known simply as 3SB), as reported in Rote *et al.*, 1993 and WO 00/02584, effectively competes with the 3G4 antibody for binding to PS, such as determined using an ELISA as recited in the claims of the captioned patent application.

6. I am providing the present Declaration and providing the attached evidence to demonstrate that the 3SB antibody does not effectively compete with the 3G4 antibody for binding to PS in an ELISA as recited in the claims of the captioned patent application.

7. Evidence of the fact that 3SB does not effectively compete with 3G4 for binding to PS in such an ELISA is presented in **Exhibit B**, which shows the results of an ELISA competition study using the 3SB and 3G4 antibodies.

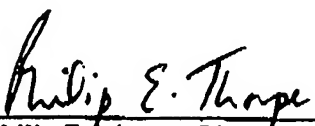
8. The data of **Exhibit B** were generated from a competitive binding ELISA, in accordance with those described in the captioned patent application. In order to detect bound 3G4 antibody, as distinct from any 3SB, a chimeric form of the 3G4 antibody (ch3G4) was used in which the mouse variable regions are linked to human IgG constant regions. Chimeric 3G4 binds to PS in the same manner as murine 3G4, by virtue of the mouse variable regions, but can be detected and differentiated from the 3SB antibody (mouse IgM) by using a detection agent specific for the human constant regions. The competitive assay was conducted as follows. The ELISA plate was coated with PS and blocked with 10% FBS. ch3G4 was kept constant at 6.67 nM, and titrated down with 3SB, starting at 100 nM. Bound ch3G4 was detected with goat anti-human IgG-HRP. An isotype-matched mouse IgM antibody of irrelevant specificity (GV39M) was used as a control for 3SB.

9. As shown in **Exhibit B**, the addition of increasing amounts of the 3SB antibody does not result in any detectable reduction in binding of the ch3G4 antibody to PS (ch3G4 binding remains essentially constant at 100% in the presence of increasing amounts of 3SB, very similar to the results using the control antibody). This demonstrates that 3SB does not effectively compete with 3G4 for binding to PS.

10. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the captioned patent application or any patent issued thereon.

July 9, 2007

Date

  
Philip E. Thorpe, Ph.D.

# EXHIBIT A

## **Curriculum Vitae - EXHIBIT A**

Name: Philip Edward THORPE

Place of Birth: Smethwick, Worcestershire, U.K.

Nationality: British (with U.S. Permanent Residency)

Home Address: 5510 Morningside Drive  
Dallas, TX 75206

Social Security #: 452-99-7852

### **EDUCATION:**

1962-1969 Moseley Grammar School, Birmingham B17, U.K.

1969-1972 University of Liverpool, U.K.

Academic Qualifications: First Class B.Sc (Hons)  
Degree in Pharmacology  
(Summa cum Laude)

### **Postgraduate Education:**

1972-1975 Medical Research Council Scholarship  
Division of Surgical Sciences  
Clinical Research Centre  
London, U.K.  
Ph.D. supervisors: Sir Peter Medawer, Dr. Stella Knight

### **POSTDOCTORAL EMPLOYMENT:**

1975-1981 Medical Research Council Fellow  
Division of Biology  
Chester Beatty Research Institute  
Institute of Cancer Research  
Royal Cancer Hospital  
Fulham Road  
Chelsea  
London SW3 6JB, U.K.

1981 - 1991 Director, Drug Targeting Laboratory  
Imperial Cancer Research Fund  
Lincoln's Inn Fields  
London WC2A 3PX, U.K.

1991 - 1998 Professor of Pharmacology  
Serena Simmons Distinguished Chair in Cancer Immunopharmacology

Department of Pharmacology and  
Hamon Center for Therapeutic Oncology Research  
University of Texas Southwestern Medical Center  
5323 Harry Hines Boulevard  
Dallas, Texas 75235-8593

1998 - 1999

Director of Oncology Research  
Associate Director of the Center for Molecular Medicine  
Maine Medical Center Research Institute  
125 John Roberts Road, Suite #5  
South Portland, Maine 04106

1999 – present

Professor of Pharmacology  
Serena Simmons Distinguished Chair in Cancer Immunopharmacology  
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#### **UT SOUTHWESTERN GRADUATE PROGRAM APPOINTMENTS:**

Cell Regulation Graduate Program, UTSW  
Immunology Graduate Program, UTSW

#### **GRADUATE SCHOOL TEACHING (annual):**

Mechanisms of Drug Action Course (Director)  
Medical Pharmacology Course  
Human Biology and Disease Course  
Cancer Biology Course  
Physician's Assistant Course

#### **UT SOUTHWESTERN COMMITTEES**

Promotion and Tenure Committee, 1997-98  
Graduate Admissions Committee, 1994-96  
Clinical Research Scientific Review And Monitoring Committee, 1997-8  
Department of Cell and Molecular Biology Review Committee, 1997-8  
Radioactive Drug Research Committee, 2003-present  
American Cancer Society Institutional Review Group, 2004-present

## **PROFESSIONAL SOCIETIES:**

American Association for Cancer Research  
American Association for Immunology  
American Society for Pharmacology and Experimental Therapeutics  
North American Vascular Biology Organization  
Sigma Xi  
Society for Biological Therapy

## **SCIENTIFIC ADVISORY BOARDS:**

Scientific Advisory Board, Cytopharm Inc., Munich, Germany, 1990-1996  
Scientific Advisory Board, Texcellon Inc., Dallas, TX, 1990-1993  
Scientific Advisory Board, Peregrine Pharmaceuticals, Inc., Princeton, NJ, 1993-1997  
Scientific Advisory Board, Repair, Inc., Portland, ME, 1998-2000  
Scientific Advisory Board, Peregrine Pharmaceuticals, Inc., Tustin, CA, 1997-present  
Scientific Advisory Board, Arcus Therapeutics, Inc., Boston, MA, 2000-2002  
Founding Scientist, Peregrine Pharmaceuticals, Inc., Tustin, CA

## **EDITORIAL BOARDS:**

IRCS Journal of International Research Communication, 1974-1984  
Advanced Drug Delivery Research Reviews, 1985-1992  
Antibody, Immunoconjugates and Radiopharmaceuticals, 1987-1995  
Bioconjugate Chemistry, 1989-present  
Journal of Drug Targeting, 1992-2000  
Therapeutic Immunology, 1992-present  
Angiogenesis, 1997-present  
Cancer Biotherapy and Radiopharmaceuticals, 2004-present

## **INTERNATIONAL CONFERENCES ORGANIZED:**

Co-organizer (with Dr. G. Gregoriadis), NATO meeting on Receptor Mediated Targeting of Drugs, Greece, 1983  
Vice Chairman, Gordon Research Conference on Drug Carriers in Medicine and Biology, Ventura, CA 1996  
Chairman (with Dr. Ruth Duncan), Gordon Research Conference on Drug Carriers in Medicine and Biology, Ventura, CA, 1998  
Chairman, 1<sup>st</sup> International Symposium on Vascular Targeting, Boston, MA, 2002  
Chairman, 2<sup>nd</sup> International Symposium on Vascular Targeting, Miami, FL, 2004

## **INVESTIGATIONAL NEW DRUG (IND) APPLICATIONS**

RFB4-SMPT-dgA for Treatment of B-lymphoma (with Dr. E. Vitetta), 1989  
RFT5-SMPT-dgA for Treatment of Hodgkin's Disease (with Dr. E. Vitetta), 1992  
Tarvacin<sup>TM</sup> for Treatment for Hepatitis C virus (with Peregrine Pharmaceuticals, Inc.), 2005



## **HONORS AND AWARDS:**

Pierce Immunotoxin Award, 1988

The State of Texas House of Representatives Resolution recognizing his contribution to cancer research, 1997.

American Cancer Society 'Award of Excellence', 1999

## **GRANTS (since 1991):**

### Past

Vascular Targeting: A New Approach to the Therapy of Solid Tumors; Dallas Biomedical Corporation; \$161,832 direct for the period of October 1, 1991-December 31, 1992.

Heparin-Steroid Conjugates: A New Class of Angiogenesis Inhibitors for Clinical Applications: Dallas Biomedical Corporation; \$134,613 direct for the period of October 1, 1991 to December 31, 1992.

Vascular Targeting: A New Approach to the Therapy of Solid Tumors; Elsa U. Pardee Foundation; \$64,843 for the period of May 1, 1992-April 30, 1993.

Vascular Targeting Program; Dallas Biomedical Corporation; \$119,123 direct for the period of January 1, 1993-June 30, 1993.

Recombinant Antibodies for Targeting the Vasculature of Solid Tumors; Elsa U. Pardee Foundation; \$128,658 direct for the period of June 1, 1993-May 31, 1995.

New Angiogenesis Inhibitors for the Therapy of Breast Cancer; American Cancer Society DHP-95; \$150,000 direct for the period of July 1, 1993-June 30, 1995.

Developmental project funded from Dr. John Minna's SPORE Grant 1 P50 CA709097 from the National Institutes of Health; \$20,000 direct for the period of September 1, 1996-August 30, 1997.

Holder of the Serena S. Simmons Distinguished Chair in Cancer Immunopharmacology, annual income \$60,000.

Vascular Targeting: A New Approach to the Therapy of Solid Tumors and Rheumatoid Arthritis; Anonymous Donor; \$1,666,665 direct for the period of September 1, 1992-December 31, 1997.

Mechanisms of drug action and disposition; National Institutes of Health T32-GM07062 (training grant, PI-Dr. Alfred Gilman); \$54,000 direct for the period of September 1, 1994-August 31, 1999.

Vascular Targeting Agents that Home to and Destroy or Coagulate Tumor Vasculature; Peregrine Pharmaceuticals; \$480,000 for the period of December 1, 1994-December 1, 1997.

Vascular Targeting Agents for Infarcting Lung Cancer; Advanced Research Program from the State of Texas; \$247,500 direct for the period of January 1, 1996-December 31, 1997.

Therapeutic Clotting to Destroy Solid Tumors; Advanced Technology Program from the State of Texas; \$190,579 for the period of January 1, 1998-December 31, 1999.

Angiogenesis Inhibitors for Therapy of Solid Tumors; National Institutes of Health 5-RO1-CA59569; \$781,718 direct for the period of December 15, 1993-November 30, 1999.

Collateral Tumor Targeting; Sponsored Research Agreement with Techniclone Corporation; \$1,050,000 direct for the period of April 1999-March 2001

Immunotoxins for the Treatment of Hodgkin's Disease; National Institutes of Health 5-RO1-CA54168; \$820,052 direct for the period of April 1, 1991-May 31, 2000.

Targeting the Vasculature of Solid Tumors; National Institutes of Health 1-RO1-CA74951; \$728,529 direct for the period of December 1, 1997-November 30, 2001.

Specific coagulation of tumor vasculature. Texas Technology ARP grant; \$200,000

#### Present

Novel anti-viral agents for treating Lassa fever. NIH, \$1,798,285, 2003-08.

Naked antibodies for treating cancer; Sponsored Research Agreement with Peregrine Pharmaceuticals, Inc., \$500,000 per year direct (since 1999)

Therapeutic clotting to destroy solid tumors; Gillson Longenbaugh Foundation, Houston, Texas; \$50,000 per year

Anti-angiogenic drugs for childhood brain cancer. Chesler Foundation, \$10,000 per year.

VEGF-rGel for targeting the vasculature of breast cancer ( M.Rosenblum, P.I). Dept. of Defense. \$43,000 per year for 2002-5.

Simmons Foundation, Serena S. Simmons Distinguished Chair in Cancer Immunopharmacology, \$86,000 per year.

Vascular Targeting Antibodies for Improving Chemotherapy of Prostate Cancer (P. Thorpe, PI). Department of Defense; \$210,000 per year

Synergy between anti-phosphatidylserine monoclonal antibody, 3G4 and docetaxel for treatment of breast cancer (X. Huang, PI; P. Thorpe, Co-PI), Susan Komen Foundation for Basic, Clinical and Translational Breast Cancer Research; \$200,000 per year

A strategy for enhancing the effect of radiation in the treatment of breast cancer (T. Luster, Fellowship). American Cancer Society; \$80,000 per year

## **PATENTS**

### **Issued**

1. Heterobifunctional linking agents derived from N-succinimido-dithio-alpha methyl-methylene-benzoates (Inventor: P. Thorpe)  
U.S. Patent No. 4,880,935
2. Purification of A-chain immunotoxins (Inventor: P. Thorpe)  
U.K. Patent No. 43606 P3474
3. Methods and compositions for the treatment of Hodgkin's disease (Inventors: P. Thorpe and A. Engert)  
U.S. Patent No. 5,165,923
4. Preparation and use of steroid-polyanionic polymer-based conjugates targeted to vascular endothelial cells (Inventor: P. Thorpe)  
U.S. Patent No. 5,474,765  
U.S. Patent No. 5,762,918
5. Methods and compositions for targeting the vasculature of solid tumors (Inventors: P. Thorpe and F. Burrows)  
U.S. Patent No. 6,004,554  
U.S. Patent No. 5,965,132  
U.S. Patent No. 5,855,866  
U.S. Patent No. 5,776,427  
U.S. Patent No. 5,863,538  
U.S. Patent No. 6,051,230  
U.S. Patent No. 6,261,535  
European Patent No. 0 627 940 (17 countries, including France, Germany, U.K.)
6. Antibodies that bind to endoglin (Inventors: P. Thorpe and F. Burrows)  
U.S. Patent No. 5,660,827
7. VEGF-Gelonin for targeting the vasculature of solid tumors (Inventor: P. Thorpe)  
U.S. Patent No. 6,451,312
8. Methods and compositions for the coagulation of tumor vasculature (Inventors: P. Thorpe and T. Edgington)  
U.S. Patent No. 6,093,399  
U.S. Patent No. 6,004,555  
U.S. Patent No. 5,877,289  
U.S. Patent No. 6,036,955  
U.S. Patent No. 6,749,853  
European Patent No. 0 771 216 (16 countries, including France, Germany, U.K.)  
Australian Patent No. 702250  
New Zealand Patent No. 288883  
Hungarian Patent No. 220347  
Singapore Patent No. 35823  
Mexican Patent No. 212,225

9. Tissue Factor methods, compositions and combination for coagulation and tumor treatment (Inventors: P. Thorpe, S. King and B. Gao)
  - U.S. Patent No. 6,156,321
  - U.S. Patent No. 6,132,729
  - U.S. Patent No. 6,132,730
  - European Patent No. 0 988 056 (15 countries, including France, Germany, U.K.)
  - Australian Patent No. 735187
  - New Zealand Patent No. 336720
  - Singapore Patent No. 66589
10. Cancer treatment methods using antibodies to aminophospholipids (Inventors: P. Thorpe, S. Ran)
  - U.S. Patent No. 6,406,693
  - Australian Patent No. 771224
  - New Zealand Patent No. 508950
11. Cancer treatment methods using therapeutic conjugates that bind to aminophospholipids (Inventors: P. Thorpe, S. Ran, R. Brekken)
  - U.S. Patent No. 6,312,694
  - European Patent No. 1 098 665 (15 countries, including France, Germany, U.K.)
  - Australian Patent No. 750414
  - Singapore Patent No. 78111
  - New Zealand Patent No. 508873
12. Antibody and antibody conjugate compositions and kits for selectively inhibiting VEGF (Inventors: P. Thorpe, R. Brekken)
  - U.S. Patent No. 6,342,219
  - U.S. Patent No. 6,342,221
  - U.S. Patent No. 6,416,758
  - U.S. Patent No. 6,524,583
  - U.S. Patent No. 6,676,941
  - U.S. Patent No. 6,703,020
  - Australian Patent No. 774287
  - Australian Patent No. 763954
  - European Patent No. 1 179 541
  - South African Patent No. 2001/8612
  - South African Patent No. 2001/8285

### **Pending**

44 pending regular U.S. patent applications and 186 pending international patent applications directed to compositions and methods for the diagnosis and treatment of cancer and viral infections

**PUBLICATIONS:(Total = 173 plus 1 submitted)**

1. Thorpe, P. E. and Knight, S. C. (1974) Microplate culture of mouse lymph node cells. I. Quantitation of responses to allogeneic lymphocytes and phytomitogens. *J. Immunol. Methods* **5**: 387-404.
2. Thorpe P. E., Knight, S. C. and Farrant, J. (1976) Optimal conditions for the preservation of mouse lymph node cells in liquid nitrogen using cooling rate techniques. *Cryobiology* **13**: 126-138.
3. Thorpe, P. E., Ross, W. C. J., Cumber, A. J., Hinson, C. A., Edwards, D. C. and Davies, A. J. S. (1978) Toxicity of diphtheria toxin for lymphoblastoid cells is increased by conjugation to anti-lymphocytic globulin. *Nature* **271**: 752-754.
4. Ross, W. C. J., Thorpe, P. E., Cumber, A. J., Edwards, D. C., Hinson, C. A., and Davies, A. J. S. (1980) Increased toxicity of diphtheria toxin for human lymphoblastoid cells following covalent linkage to anti-(human lymphocyte) globulin or its F(ab<sup>1</sup>)<sub>2</sub> fragment. *Eur. J. Biochem.* **104**: 381-390.
5. Davies, A. J. S., Edwards, D. C. and Thorpe, P. E. (1981) Introduction to a symposium on new trends in human immunology and cancer immunotherapy. In 'New Trends in Human Immunology and Cancer Immunotherapy'. pp 1-7.
6. Thorpe, P. E., Cumber, A. J., Williams, N., Edwards, D. C., Ross, W. C. J. and Davies, A. J. S. (1981) Abrogation of the non-specific toxicity of abrin conjugated to anti-lymphocyte globulin. *Clin. Exp. Immunol.* **43**: 195-200.
7. Thorpe, P. E., Brown, A. N. F., Ross, W. C. J., Cumber, A. J., Detre, S. I., Edwards, D. C., Davies, A. J. S. and Stirpe, F. (1981) Cytotoxicity acquired by conjugation of an anti-Thy 1.1 monoclonal antibody and the ribosome-inactivating protein, gelonin. *Eur. J. Biochem.* **116**: 447-454.
8. Edwards, D. C. and Thorpe, P. E. (1981) Targeting toxins - the retiarian approach to chemotherapy. *Trends in Biochemical Sciences*, 313-316.
9. Edwards, D. C., Smith, A., Ross, W. C. J., Cumber, A. J., Thorpe, P. E. and Davies, A. J. S. (1981) The effect of abrin, anti-lymphocyte globulin and their conjugates on the immune response of mice to sheep red blood cells. *Experientia* **37**: 256-257.
10. Skilleter, D. N., Paine, A. J. and Thorpe, P. E. (1981) Selective direction of ricin to hepatic parenchymal cells. *Biochem. Soc. Transactions* **10**: 122-123.
11. Thorpe, P. E., Cumber, A. J., Davies, A. J. S., Edwards, D. C., Ross, W. C. J. and Smith, A. (1982) The immunosuppressive effects of anti-Thy 1.1 F(ab<sup>1</sup>)<sub>2</sub> conjugated to abrin. In 'Antibodies as Carriers of Anticancer Drugs or Toxins: Quo Vadis?' (F. K. Jansen and R. Roncucci, eds.) SANOFI, Montpellier, France, pp. 134-135.
12. Thorpe, P. E., Brown, A., Cumber, A. J., Davies, A. J. S., Edwards, D. C., Ross, W. C. J. and Stirpe, F. (1982) Selective cytotoxicity with a conjugate of anti-Thy 1.1 antibody and gelonin.

In 'Antibodies as Carriers of Anticancer Drugs or Toxins: Quo Vadis?' (F. K. Jansen and R. Roncucci, eds.) SANOFI, Montpellier, France, pp. 123-124.

13. Edwards, D. C., Ross, W. C. J., Cumber, A. J., McIntosh, D., Smith, A., Thorpe, P. E., Brown, A., Williams, R. H. and Davies, A. J. S. (1982) A comparison of the in vitro and in vivo activities of conjugates of anti-mouse lymphocyte globulin and abrin. *Biochim. Biophys. Acta* **71**: 272-277.
14. Edwards, D. C., Thorpe, P. E. and Davies, A. J. S. (1982) Antibody-toxin conjugates as potential therapeutic agents. In 'Targeting of Drugs' (G. Gregoriadis, J. Senior, and A. Trouet, eds.) Plenum Press, N. Y. and London, pp. 83-96.
15. Thorpe, P. E., Ross, W. C. J. (1982) The preparation and cytotoxic properties of antibody-toxin conjugates. *Immunol. Rev.* **62**: 119-158.
16. Thorpe, P. E., Edwards, D. C., Davies, A. J. S., Ross, W. C. J. (1982) Monoclonal antibody-toxin conjugates: aiming the magic bullet. In 'Monoclonal Antibodies in Clinical Medicine' (A. McMichael and J. Fabre, eds.) Acad. Press, London, pp. 167-201.
17. Thorpe, P. E., Mason, D. W., Brown, A. N. F., Simmonds, S. J., Ross, W. C. J., Cumber, A. J. and Forrester, J. A. (1982) Selective killing of malignant cells in a leukaemic rat bone marrow using an antibody-ricin conjugate. *Nature* **297**: 594-596.
18. Mason, D. W., Thorpe, P. E., Ross, W. C. J. (1982) Elimination of leukaemic cells from rodent bone marrow in vitro with antibody-ricin conjugates: implications for autologous marrow transplantation in man. *Cancer Surveys* **1**: 389-415.
19. Davies, A. J. S., Jansen, F. K., Olsnes, S., Thorpe, P. E., Wofsy, L. and Edwards, D. C. (1982) Antibodies as toxin carriers in cancer immunotherapy. In 'Current Chemotherapy and Immunotherapy' (Proceedings of the 12th Int. Congress of Chemotherapy, Vol. 2) (Periti, P. and Grassi, G. G. Eds.) pp. 1141-1143.
20. Thorpe, P. E., Brown, A., Foxwell, B. and Myers, C. (1983) Blockade of the galactose-binding site of ricin by its linkage to antibody. In 'Monoclonal Antibodies and Cancer' (B. D. Boss, R. Langman, I. Trowbridge and R. Dulbecco, eds.) Acad. Press (London) Ltd., pp. 117-124.
21. Vodinelich, L., Myers, C., Sutherland, R., Thorpe, P. E. and Greaves, M. F. (1983) WT1: a monoclonal antibody in T-cell acute lymphoblastic leukemia. *Leukemia Reviews International* **1**, 263.
22. Thorpe, P. E., Detre, S. I., Mason, D. W., Cumber, A. J. and Ross, W. C. J. (1983) Monoclonal antibody therapy: 'model' experiments with toxin conjugated antibodies in mice and rats. *Haematology and Blood Transfusion* **28**: 107-111.
23. Rennie, D. P., McGregor, A. M., Wright, J., Weetman, A. P., Hall, R. and Thorpe, P. E. (1983) An immunotoxin of ricin A chain conjugated to thyroglobulin selectively suppresses the antithyroglobulin autoantibody response. *Lancet* **ii**, 1338-1340.
24. Thorpe, P. E., Ross, W. C. J., Brown, A. N. F., Myers, C. D., Cumber, A. J., Foxwell, B. M. J. and Forrester, J. A. (1984) Blockade of the galactose-binding sites of ricin by its linkage to

antibody: specific cytotoxic effects of the conjugates. *Eur. J. Biochem.* **140**: 63-71.

25. Sikora, K., Smedley, H. and Thorpe, P. E. (1984) Tumor Imaging and Drug Targeting. *Brit. Med. Bull.* **40**: 233-239.
26. Myers, C. D., Thorpe, P. E., Ross, W. C. J., Cumber, A. J., Katz, F. E., Tax, W., and Greaves, M. F. (1984) An immunotoxin with therapeutic potential in T cell leukemia: WT1-ricin A. *Blood* **63**: 1178-1185.
27. Foxwell, B. M. J., Ross, W. C. J. and Thorpe, P. E. (1984) Antibody-ricin conjugates: a method of linkage which blocks the galactose binding site of ricin. *Behring Inst. Mitt.*, **74**: 101-107.
28. Thorpe, P. E. (1984) Antibody-toxin conjugates as anti-cancer agents. In 'Cancer Chemotherapy and Selective Drug Development' (Harrap, K. R., Davies, W. and Calvert, A. H. eds.) Martinus-Nijhoff Publishing Co., Boston, The Hague, Dordrecht and Lancaster, pp. 263-267.
29. Paraskeva, C., Buckle, B. G. and Thorpe, P. E. (1985) Selective killing of contaminating human fibroblasts in epithelial cultures derived from colorectal tumours using an anti-Thy-1 antibody-ricin conjugate. *Br. J. Cancer* **51**: 131-134.
30. Foxwell, B. M. J., Detre, S. I., Donovan, T. A. and Thorpe, P. E. (1985) The use of anti-ricin antibodies to protect mice intoxicated with ricin. *Toxicology* **34**: 79-88.
31. Cumber, A. J., Forrester, J. A., Foxwell, B. M. J., Ross, W. C. J. and Thorpe, P. E. (1985) The preparation of antibody-toxin conjugates. *Methods in Enzymology* **112**: 207-224.
32. Thorpe, P. E., Detre, S. I., Foxwell, B. M. J., Brown, A. N. F., Skilleter, D. N., Wilson, G., Forrester J. A. and Stirpe, F. (1985) Modification of the carbohydrate in ricin with metaperiodate-cyanoborohydride mixtures: effects on toxicity and in vivo distribution. *Eur. J. Biochem.* **147**: 197-206.
33. McIntosh, D. and Thorpe, P. (1985) Role of the B-chain in the cytotoxic action of antibody-ricin and antibody-abrin conjugates. In 'Receptor-Mediated Targeting of Drugs' (Gregoriadis, G., Poste, G., Senior, J. and Trouet, A. eds.) NATO ASI Series A, **82**: 105-118.
34. Foxwell, B. M. J., Donovan, T. A., Thorpe, P. E. and Wilson, G. (1985) The removal of carbohydrates from ricin with endoglycosidases H, F, and D and  $\forall$ -mannosidase. *Biochim. Biophys. Acta* **840**: 193-203.
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# **EXHIBIT B**

